indicated a readiness to consider additional pilot projects; the committee then selected two more proposals prepared by Russian investigators that it considered interesting. These proposed projects, which are also included in Box E-1, are currently being processed by the ISTC.

With regard to the goals of the pilot projects set forth earlier, the decision to fund six projects at the beginning of the study proved sound for several reasons:

- Lessons learned about the roles of Russian ministries and institutions and of the parties to the ISTC in the development, approval, and implementation of these projects have been important in formulating the recommendations in this report. Also, the projects provide a base of experience that can assist in designing and implementing more ambitious projects.
- The projects provide an opportunity for U.S. and Russian scientists to establish personal contacts that will help sustain and expand research relations.
- The research topics are of considerable interest in Russia and the United States with regard to both scientific advancement and practical applications. Ties to health authorities and to industry, as well as to scientific institutions, are an important aspect of some of the projects.
- The projects test the practical aspects of transparency, with scientist-to-scientist contacts playing a significant role in this regard. Transparency is important for providing increased assurance that joint work on dangerous pathogens is not being misused to provide technical contributions to illegitimate BW-related activities.
- Reciprocal access to laboratories within the context of these projects offers new insights about biotechnology activities in key Russian facilities—an important contribution to confidence building.

Selection of the Institutes

Given the short lead time available for establishing these projects, the NAS committee, with DOD concurrence, decided to locate them at the State Research Center for Applied Microbiology in Obolensk and the State Research Center for Virology and Biotechnology, "Vector" in Koltsovo. This decision was based on the following considerations:

- As a result of the important roles the two institutes played in the BW program of the former Soviet Union, they have some of the strongest research capabilities related to dangerous pathogens in the country.
- These institutes have strong linkages with other institutes of the Biopreparat complex, institutes of MOD, and other institutes with capabilities related to dangerous pathogens. Therefore, they provide good initial points of entry in the development of a program of national scope.
- Through previous NAS activities in Russia, committee members were personally acquainted with the directors and other personnel of the two institutes and believed that they would be receptive to projects involving active bilateral collaborators.
- ISTC had been successful in initiating a few projects at the two institutes, beginning in 1994, which indicated that these institutes were prepared to overcome administrative hurdles in developing cooperative activities and would agree to provide access to their facilities.

In short, the two institutes are important in terms of their capabilities, experience, and organizational links to the former Soviet BW complex and to public health. In addition, they were ready to quickly initiate projects involving U.S. collaborators.

Selection of the Initial Projects

In late 1996, small teams of committee members and staff visited Obolensk and Koltsovo, where they reviewed proposals and consulted with leaders of the institutes and principal investigators of

proposed projects. They also made preliminary assessments of some capabilities of the institutes. These teams developed their project recommendations, taking into account the constraints of limited funds and the need to complete the projects by September 1998.

Obtaining early experience that would be useful in developing the long-term program was an important purpose of the projects. Thus, it was desirable to have the projects operational as soon as possible. This requirement meant that Russian institutes needed to have formal government approvals in hand or that this approval could be obtained easily. Therefore, a number of promising but yet-to-be-approved proposals prepared by the institutes were excluded from consideration because a delay of several months could be anticipated for both scientific and security reviews in Moscow. The committee recommends that some of these proposals be given priority for consideration in the *Pathogens Initiative*. However, the committee also strongly recommends that U.S. participants adopt a more proactive role in identifying possible topics and proposals for funding under the initiative now that the time constraints of the past year are diminished.

The committee approved the recommendations of its members who had visited the institutes and developed the following criteria for project selection during the course of its deliberations:

- Importance of the topic: the project will make an important contribution to the epidemiology, prevention, diagnosis, or therapy of any disease that is associated with dangerous pathogen(s) or that is (1) historically linked with BW applications or (2) a source of substantial public health concern. If successful, the project will open up a new area of important research on dangerous pathogens.
- Quality of the proposal: the project is scientifically and technically sound; anticipated results are clear; the project is feasible; there is a strong work plan; budget and manpower estimates are appropriate; and there are measurable milestones.
- Quality or capacity of the principal investigator, research team, and facilities: the proposing laboratory must have strong technical capabilities in the general research area, and the personnel and facilities proposed must have adequate capabilities to carry out the project.
- Provision for strong U.S. collaboration: the project involves a topic that will attract strong and relevant U.S. expertise, and the commitment of the U.S. collaborator(s) is clear.
- Engagement of former Soviet BW expertise: the project involves former or current defense scientists, or facilities or it provides important contributions to a larger program that involves such scientists or facilities.
- Promotion of transparency: the project meets standard ISTC access criteria, and reciprocal laboratory visits between collaborators are an integral aspect. Projects that meet such criteria and also offer access to facilities or personnel not previously engaged in collaborative projects are of particular interest.

The selected projects scored high when measured by the foregoing criteria. Also, in considering these and other aspects of each project, the committee made the judgment that the project's potential contributions to public health or U.S. national security interests outweighed the potential risk that it might contribute to the development or improvement of offensive BW capabilities.

Use of the ISTC Mechanism

The committee decided that the ISTC was the best mechanism to use for entering into agreements with the Russian institutes and for transferring funds to them. Because the objectives of the initial projects were entirely consistent with its purpose, the ISTC formally accepted NAS as one of its

partners. This status enabled the Academy to use well-established and reliable international mechanisms to develop and implement the projects.[1]

Reliance on the ISTC solved many problems encountered in supporting research activities in Russia, including issues of foreign access to project sites, sharing of intellectual property rights, allowable costs, financial auditing, reporting requirements, overhead charges, wage scales, and exemptions from taxes and customs fees. In all of these areas, NAS adopted standard ISTC approaches that were also fully acceptable to the two Russian institutes and to the U.S. and Russian governments. Of special importance is the ISTC procedure of providing funds for salaries directly to individual researchers, thereby circumventing opportunities for intermediaries to divert a portion of these funds.

The committee now feels even more strongly about the correctness of its decision to use the ISTC mechanism in light of reports that some U.S. agencies have employed other mechanisms that lack special waivers associated with handling funds for scientific research and, as a result, have lost up to 50 percent of their funding to Russian tax collection and pension accounts.[2] Perhaps a broadly based bilateral agreement between the two countries can address these issues, but in the absence of such an agreement the ISTC remains an important institution for facilitating joint projects.

Value Added by the NAS Committee

In working with ISTC staff and reviewing related ISTC projects, the committee recognized that it could offer value added to the usual approach of the ISTC. In general, the governments that are parties to the ISTC agreement have had little influence over the proposals related to dangerous pathogens that Russian institutes have chosen to submit for consideration; they have simply considered any proposals that are submitted to the ISTC. These governments have then searched for appropriate collaborators for the most interesting proposals, relying on the collaborators to obtain their own funds for active participation in the projects.

Value added by the NAS was reflected in the following:

- U.S. specialists selected by the Academy were involved not only in choosing the research topics to be developed into fundable proposals but also in modifying the research plans. Therefore, the NAS was in a strong position to ensure that proposals were oriented toward priority scientific interests of the United States as well as toward Russian interests. Also, the early involvement of U.S. specialists improved the quality of the proposals submitted for approval to both the committee and the U.S. government as an ISTC party.
- The committee includes leading U.S. scientists in the fields of interest, with experience in research directly related to biological defense. Therefore, it was in a good position to critically review not only technical merit but also linkages to BW, including the potential contribution of research projects to offensive BW capabilities.
- In view of the committee's extensive connections with the U.S. research community, it was able to enlist U.S. collaborators who are well qualified for the tasks and, recognizing the direct benefits of collaboration, highly motivated to work closely with the Russian teams throughout the lifetimes of the projects.

---

[1] In 1996 the parties to the ISTC decided to encourage other government and nongovernment organizations with access to financial resources to use its legal, management, and financial frameworks for developing and implementing projects that are consistent with ISTC objectives. The U.S. government recommended that the ISTC accept NAS as a partner for supporting cooperative activities directed to dangerous pathogens. Projects proposed by the Academy are thus subject to the review and approval of the U.S., Japanese, and Russian governments and the European Union during ISTC deliberations.

[2] See Lelyveld, M. S. 1997. Skimming Cuts Aid to Russian Scientists. *Journal of Commerce* May 13.

- The committee and staff have extensive experience in developing and reviewing proposals and are skilled in translating Russian concepts into proposal language that is easily understandable in the West. Thus, they were able to substantially reduce the lengthy development time required for most ISTC projects. The usual time needed to launch an ISTC project includes 6 to 12 months to develop a fundable proposal and an additional 6 to 9 months from ISTC acceptance of a fundable proposal until the operative commencement date of the project—a total of 12 to 21 months. The required time to launch the six pilot projects included three months for the Russian institutes to prepare fundable proposals and three months from the date of submission to ISTC until the operative commencement dates.

INSIGHTS FROM THE PILOT PROJECTS

Although the pilot projects are still in the early stages of implementation, a few lessons have been learned in developing them that are important in considering future activities.

- Despite the loss of hundreds of scientists and decline in the quality of laboratories and equipment, each of the two Russian institutes retains a few hundred skilled scientists and strong capabilities to conduct important research. The State Research Center for Virology and Biotechnology has a larger staff and more diverse facilities than the State Research Center for Applied Microbiology.
- As of June 1997, the two institutes had more than 100 unfunded proposals of highly variable quality. Some had been submitted to funding agencies in Russia and abroad, and others were still in the institutes awaiting indications of even minimal interest from funding sources. Although some proposals appear attractive for cooperative research efforts, a number of the most interesting ones involving dangerous pathogens still require formal approval of the Russian government, which may take three to six months or longer.
- The institutes have only limited e-mail capabilities and do not have regular access to the World Wide Web.
- The institutes attach great importance to having active U.S. collaborators working on their projects. In addition to benefiting from collaboration during the projects, institute leaders believe that foreign collaborators can assist in securing funds to expand projects into related areas of interest to the institutes. Effective collaborators have been the exception rather than the rule, however, with foreign-funded projects at the institutes.
- The institutes consider the ISTC the best mechanism for distributing foreign funds within Russia. As previously noted, some U.S. experiences with other mechanisms have been less satisfactory for a variety of reasons, such as loss of funds to central offices in Moscow, customs problems, and taxes imposed at the local level. At the same time, sending equipment, supplies, and samples from abroad to research institutes in Russia, even through ISTC channels, will be complicated.
- Although the two institutes have long-standing ties with institutes of the MOD and other institutes in the civilian sector, they seldom propose multi-institute projects for foreign financing, because this adds to administrative complications. In particular, MOD has not yet been involved in research projects that require giving foreign collaborators access to research laboratories at military facilities.

As the pilot projects proceed, other insights undoubtedly will be gained. The hands-on experiences of U.S. and Russian collaborators will be of special interest, in both hosting colleagues and working in the laboratory facilities of those colleagues.

PRINCIPLES TO GUIDE BILATERAL COOPERATION

Based on the committee's consultations with Russian colleagues and the experience gained in the pilot projects, three overarching principles were developed to guide future bilateral activities directed toward dangerous pathogens. These principles also appear relevant to other cooperative programs that engage specialists from the former Soviet BW complex. Broad acceptance of such principles will reduce confusion in Washington and Moscow about approaches that are appropriate in this sensitive area and will help ensure that approaches used in different programs are mutually reinforcing.

1. Projects should be collaborative in design and conduct.

- Only projects that are of interest to specialists in both countries should be undertaken. There are not sufficient funds to support all activities proposed, and an important criterion for project selection is the level of support among specialists in both countries for pursuing the proposed activities. A measure of this interest is the extent of collaboration included in the implementation of a project.
- All projects should be conducted on the basis of cooperation, not assistance, with each side making intellectual, financial, and in-kind contributions. Carrying out projects that are designed as part of foreign assistance activities, or are perceived as such could lead to misconceptions that limit political support for such activities. Further, both countries have much to contribute, and although the Russian contribution may be largely intellectual at this time, this intellectual resource warrants the label of cooperation on projects.
- All relevant constituencies in both countries should be able to apply for participation in the program. Bilateral programs will never be large enough to include all interested and important U.S. and Russian specialists. However, the individual activities should be as encompassing as possible, and competition for financial support should be open to all qualified specialists.

2. Projects should be designed and conducted in a way that maximizes transparency.

- Activities should be carried out in an environment of openness. Free exchange of information between participants in cooperative activities is central to achieving both scientific and national security objectives. Transparency begins at the project level and should be based on regular and sustained contacts between U.S. researchers and their Russian counterparts and on regular visits to facilities where the research is carried out. In this regard the ISTC has developed guidelines for access to facilities at the project level (Box 1-2). Although limited, these guidelines are a good initial basis for cooperation. In time, the broader concept of transparency described in Chapter 1 should encompass a wider range of research activities at the institute level.
- Direct contacts among specialists should be stressed. Given the sensitivity of the topic, government officials in both countries should be involved in the development and approval of projects. However, once a program has demonstrated that it will be managed responsibly, governments should minimize interference. In short, they should be promoters of responsible cooperation but should give the cooperating scientists maximum flexibility once the ground rules for cooperation have been established.
- A central coordination point in each government should be apprised of anticipated cooperative activities. Given the increasing number of bilateral efforts, it is essential for central offices to have up-to-date information on such activities. Because the same scientists may be participating in projects under the auspices of different cooperative programs, such a registry will be most useful if it includes all cooperative activities involving defense scientists.

3. Results of cooperative projects should be disseminated to the widest possible interested audience.

- Whenever possible, research results should be promptly published or made available to international audiences through other channels. A critical aspect of international science is sharing project results. Prompt and broad distribution of findings should have beneficial effects in encouraging

reciprocal sharing of information that helps prevent the unnecessary duplication of research activities while broadening transparency.

- Intellectual property and sensitive findings should be protected. Notwithstanding the desirability of wide dissemination of research results, scientists working with dangerous pathogens that have BW potential have a special responsibility to ensure that, in accordance with the Biological Weapons Convention, sensitive information is not disseminated to irresponsible parties. Also, researchers should be able to protect information that has commercial value. Mechanisms should be developed to help ensure an appropriate balance between the free flow of scientific information and limitations based on these two legitimate reasons for restricting the dissemination of information in certain cases.
- Intellectual property rights resulting from cooperative activities should be shared by the participating institutions on fair and equitable terms. As cooperative projects develop, mutual confidence that project collaborators will not misuse intellectual property should increase; to this end, project agreements should include appropriate provisions for the rights to such intellectual property. The provisions of the ISTC model project agreement set forth in Box 2-2 provide a point of departure for considering arrangements for specific projects.

Box 2-2 Highlights of ISTC Provisions on Intellectual Property Rights

- All rights to research results reside with the Russian institution that carries out a project.
- All ISTC parties are entitled to no-cost licenses to use research results for noncommercial purposes.
- The financing party is entitled to a no-cost exclusive license to use research results for commercial purposes in its territory.
- The Russian institution may use research results for commercial purposes in other areas of the world or may be compensated for licenses for such use.
- The financing party and the Russian institution may agree on alternative arrangements.

Source: ISTC Statute, Article XIII, March 17, 1994.

ORGANIZING RESEARCH ACTIVITIES IN THE FUTURE

Critical aspects of near-term cooperation will be the criteria used to select the most promising joint projects, the size and scope of individual projects, and the financial arrangements for supporting the projects.

Criteria for Judging Research Proposals

The criteria developed during assessments of the pilot projects and set forth previously in this chapter are appropriate for evaluating the merits of future projects. The following two criteria are also important if an expanded program is initiated:

1. Likelihood of sustainability: the project should be of interest to commercial, government, or other organizations that want to build on the research results and have the financial means to continue supporting research in the general field after project completion. Many aspects of research on dangerous pathogens are considered to be within the public health responsibilities of governments; therefore public funds are undoubtedly needed to continue activities in a number of areas. However, in some areas such as diagnostic devices and vaccines, efforts to interest commercial organizations in providing financial support are essential.

2. Promotion of linkages between defense scientists or facilities and civilian scientists or facilities: new internal networks should be reflected in project activities. Although defense scientists are very capable, some civilian institutions have more extensive experience and official responsibilities in addressing public health problems. In some cases, multi-institutional projects involving specialists from

both communities may be appropriate; in other cases, complementary projects may be the preferred course. In either case, joint planning and coordination activities should contribute to project success and bring the two communities closer together.

Size and Scope of Research Projects

In general, future projects should be larger and longer in duration than the pilot projects. The ISTC has had quite positive experience in supporting larger projects that reflect the importance of keeping research teams together. Also, establishing large numbers of small projects entails high administrative costs. Three-year projects involving teams of about 10 Russian specialists appear to be appropriate. At the same time, flexibility for supporting smaller or larger projects, depending on specific research objectives, is important.

Financial Realities

Each side should cover its own expenses associated with cooperation to the extent possible, with equal sharing of all costs as the long-term objective. Given current financial difficulties in Russia and the fact that monetary support is only one type of contribution to a collaborative project, the following approach for covering costs of collaboration in the near term appears appropriate:

1. For cooperative research projects,
   - The United States should cover costs in the United States; and
   - The United States should contribute to costs in Russia in accordance with ISTC regulations about allowable costs (e.g., salaries; equipment; supplies; travel; and technician, computing, and support costs unique to the project) and should pay the expenses of U.S. collaborators in Russia, with Russia covering other facility, administrative, and indirect costs.
2. For technical meetings and workshops in Russia,
   - The United States should cover the expenses of U.S. participants;
   - Russia should cover the expenses of Russian participants; and
   - Both should share additional costs associated with events.
3. For technical meetings and workshops in the United States,
   - Russia should cover the costs of international travel; and
   - The United States should cover all other costs.

A GOOD BASIS FOR FUTURE COOPERATION

The activities of this committee, together with related efforts of U.S. agencies, have generated considerable interest and growing support in Russia among the community of former and current defense scientists in joint projects with U.S. specialists directed to the biological sciences and biotechnology. Joint projects directed to dangerous pathogens should be an important subset of such cooperation.

With the transfer to Russian institutes and U.S. collaborators of approximately $500,000, six pilot projects are under way; two others are in the final stages of development. The process of developing these projects and their first few months of activity are demonstrating that collaborative efforts operated under expert guidance and within an effective administrative framework can engage key Russian defense scientists, attract excellent U.S. partners in academia and government, and support joint work on high-priority topics with the potential to achieve significant benefits.

In addition to the costs of supporting research activities at the two Russian institutes and the travel and related expenses of U.S. collaborators, significant costs have been incurred in developing the

pilot projects and in establishing the base for future cooperation, including joint planning activities with Russian colleagues. However, the percentage of total funds devoted to such supporting activities will decrease sharply if an expanded cooperative program is pursued, as set forth in Chapter 3.

In summary, the recent experience of the committee confirms that despite current political uncertainties and economic difficulties in Russia, it is feasible to implement important cooperative programs involving Russian defense scientists that serve the national security, public health, economic development, and scientific objectives of both countries as set forth in Chapter 1.

3

◆ ◆ ◆ ◆ ◆

Phase 1: A *Pathogens Initiative* to Expand Cooperation

A WINDOW OF OPPORTUNITY FOR INITIATING JOINT EFFORTS

The recent activities initiated by the National Academy of Sciences (NAS) in Russia and discussed in Chapter 2 have helped open a window of opportunity for engaging significant elements of the former Soviet biological weapons (BW) community in joint projects of public health significance directed to dangerous pathogens. As evidenced by the major time commitments of key Russian specialists in working with the NAS committee and staff, Russian officials and scientists are clearly interested in expanding cooperative endeavors in the near future.

Meanwhile, ISTC support of projects at Biopreparat research institutes is increasing, and the Department of Energy (DOE) recently announced a new program for supporting former Soviet BW specialists under the auspices of the Initiatives for Proliferation Prevention (IPP). These developments have added to the desires of the Russian scientific community for expanded cooperation that includes infusions of financial resources from abroad.

Russian readiness to expand cooperation involving one of the most sensitive components of the former Soviet military establishment can be attributed to a variety of other developments as well, including the following:

- As Biopreparat seeks new roles for providing services to the Ministry of Health and producing items for the civilian market, its research institutes–after favorable initial experiences with the International Science and Technology Center (ISTC) projects and limited success with foreign companies–are increasingly interested in participating in public health efforts with foreign partners.
- Many Russian nuclear research institutes and production enterprises have participated effectively in international programs, including organizations that have been involved in sensitive activities; leaders of the biological defense community are interested in establishing analogous international programs.
- The Ministry for Science and Technology has assumed increasing responsibility for financing and approving civilian activities at institutes that, in Soviet times, were involved in BW-related research; the ministry's interest in the benefits of international cooperation is well known throughout the Russian scientific community.
- The autonomy of political leaders is increasing in regions of Russia where research and related facilities involved in former Soviet BW efforts are located. Most regional leaders want to capitalize on the advanced technological capabilities of such facilities to promote educational opportunities and economic growth. It is likely that a number of regional governors recognize the importance of foreign partnerships in achieving this goal. As one example, the Communist governor of the Kirov region indicated to committee members a readiness to encourage such cooperation in biotechnology.
- In government agencies in Moscow and at some research institutes, international cooperation, including scientific cooperation, in combating bioterrorism that could strike Russia is a topic of increasing interest.

As noted previously, resistance to international cooperation persists within the Ministry of Defense (MOD). However, MOD apparently has not objected to Biopreparat's outreach, and some well-informed Russian colleagues believe that in the future, MOD will allow its institutes to join in cooperative efforts. Also, the interest of the Russian Defense Council in promoting cooperation and its reported endorsement of the NAS activity are encouraging.

Biopreparat institutes and enterprises were a major component of the former Soviet BW complex. Effective engagement of Biopreparat specialists and institutes therefore warrants a substantial bilateral effort even if MOD remains reluctant to participate.

Although Russian interest in cooperation is increasing, the future political course within Russia remains difficult to predict, and curtailment of bilateral cooperation with the United States in sensitive areas could be among the early targets if a reversal of the current movement toward political and economic reform occurs. As cooperation becomes more ingrained in the scientific community, joint efforts are more likely to survive severe political shocks, which underscores the importance of establishing and broadening such cooperation as soon as possible.

In view of the foregoing considerations, the committee believes that prompt action to follow up on recent steps toward expanded bilateral cooperation is very important.

RECOMMENDATION FOR A *PATHOGENS INITIATIVE*

Drawing on its positive experiences during 1996 and 1997 and current Russian interest in expanding cooperation, the committee recommends that a *Pathogens Initiative* focused on the public health aspects of dangerous pathogens begin as soon as possible. It will substantially expand the initial program of pilot projects described in Chapter 2 and will build on the limited efforts of several U.S. government agencies in this specialized field as presented in Table E-1.

If the Department of Defense (DOD) decides to support a *Pathogens Initiative*, as recommended in this report, the program will provide significant civilian research opportunities for defense scientists. The assurance of regular paychecks will reduce the economic incentives for these scientists to look elsewhere for financial support, including states of proliferation concern. Thus, the program will directly support DOD's mission to prevent diffusion of critical technical know-how that could assist in developing BW capabilities.

The core of a *Pathogens Initiative* should be joint research projects directed to the epidemiology, prophylaxis, diagnosis, and therapy of diseases associated with dangerous pathogens, as well as related fundamental research. The approaches for selecting and administering such projects developed during the implementation of pilot projects, described in Chapter 2, should serve as the initial framework for an expanded research program.

The *Pathogens Initiative* is projected to last five years, beginning in fiscal year (FY) 1998. The research and other components involved are discussed below. As the program matures, additional activities may be included and some recommended activities and approaches may be modified to reflect the experience gained.

If successful, the *Pathogens Initiative* should lead quite naturally to a state of sustained, transparent cooperation with Russia. This cooperation should be at a level of activity that provides attractive opportunities for a significant number of specialists from each country while at the same time concentrating research at a limited number of high-quality facilities in Russia. A favorable political environment is necessary, and the joint efforts envisaged should, in turn, contribute to improved bilateral political relationships. A possible template for sustained cooperation as a follow-up development to the *Pathogens Initiative* is presented in Chapter 4.

Organizational Structure

If a *Pathogens Initiative* is undertaken, the topic of expanded bilateral cooperation directed toward dangerous pathogens should be considered and endorsed at the intergovernmental level at an early date.

When the committee began discussing cooperation with Russian colleagues during the fall of 1996, Russian officials and scientists advocated prompt consideration of the initiative by the Gore-Chernomyrdin Commission (GCC). They argued, in particular, that endorsement at the intergovernment level would strongly encourage MOD to become involved and would help resolve many of the policy, implementation, and budget issues confronting other participating Russian organizations.

The pilot projects did not appear to constitute a sufficiently robust program to warrant consideration at the GCC level during 1997. Also, these projects could be implemented quickly through the ISTC with little need for political endorsement at a higher level. However, an expanded program will raise the political as well as scientific stakes considerably, and intergovernment endorsement could be helpful in providing impetus for an expansion in addition to encouraging coordination among related bilateral efforts.

The committee believes that the strong support of both governments is important for successful implementation of a *Pathogens Initiative.* It recommends that the two governments provide political support for such a program through the GCC or through another appropriate intergovernmental mechanism.

In addition to obtaining intergovernment endorsement of the *Pathogens Initiative*, the U.S. government should support a well-qualified technical working group to meet regularly with the Russian working group established by Biopreparat in the spring of 1997 to interact with the committee. The two working groups could address many of the details of cooperation for presentation to both governments. The suggestions of the Russian working group thus far have been constructive and realistic. The initial membership of the Russian working group is set forth in Box 2-1.

A *Pathogens Initiative* also should be accompanied by a stronger mechanism within the U.S. government for coordinating technical programs that involve cooperation with former Soviet BW specialists, including joint research on dangerous pathogens. Several organizations—including the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Food and Drug Administration (FDA), and U.S. Department of Agriculture (USDA)—have special technical capabilities that should be combined with nongovernment scientific capabilities to provide a focal point for coordination of scientific and technical aspects of the program. This coordinating body could greatly facilitate coordination of the *Pathogens Initiative* with closely related activities carried out through other U.S. government channels such as the ISTC and IPP. Coordination of these activities should also extend to global programs of infectious disease prevention and control, such as the World Health Organization (WHO) Division of Emerging and Other Communicable Diseases, Surveillance and Control (EMC).

An important concern is the possibility of a downturn in U.S.-Russian relations that is so severe it requires the termination of cooperative efforts. If such a change came abruptly, little could be done to safeguard against possible diversion of Russian expertise to prohibited activities. However, if Russian performance of the project agreements became impossible, the U.S. could terminate the agreements with 30 days notice and retrieve unspent funds.

Research Collaboration

The lessons learned in selecting, developing, and implementing the six pilot projects serve as important building blocks for the program. In particular, they suggest important new directions for collaboration. For example, at the beginning of deliberations, the committee hesitated to become too deeply involved with pathogens that have been historic BW agents. However, as discussed in Chapter 1, it is now much clearer that investigations of pathogens with BW potential are not only feasible but desirable if the goal of mutual assurance that activities and intentions are consistent with international obligations is to be achieved. A number of leading specialists in both countries fully recognize the importance of transparency as key to preventing the dual-use issue from becoming a major impediment to such cooperation, and transparency assumes its rightful level of significance when applied to the pathogens of greatest concern.

The recommended research effort of the *Pathogens Initiative* involves 15 three-year joint projects initiated each year. This recommendation is based on the following considerations:

- Significant joint research activities should be located at the most important Russian institutions with research capabilities related to dangerous pathogens that were established in the framework of the Soviet BW program. (Although Boxes 1-2, 1-3, and 1-4 provide a list of candidate institutes, not all of them will compete successfully for joint projects.) This program should include MOD institutes when they are prepared to participate. It is estimated that from the pool of 45 active projects when the program is fully operational, an average of 3 projects will be located at each participating Russian institution. Following the pattern established during development of the pilot projects, teams of U.S. experts should visit all potential participating institutes of interest to ensure that their proposals are consistent with current capabilities.
- The 15 projects initiated each year could engage about 150 Russian researchers on a full-time basis over a period of three years, or a larger number if there are some part-time participants. Using the ISTC estimate of $10,000 to support one full-time Russian specialist in Russia per year (including salary, equipment and supplies, technician and administrative support personnel, travel, and limited overhead), the average three-year cost to the United States is estimated at $300,000 for each project. Because up to 45 projects will be active at any given time, more than 450 important Russian researchers will be participating, including a limited number of part-time participants (see Table E-2 for phasing of joint research projects). Such part-time participants will be contractually obligated to spend the remainder of their time on activities acceptable under the Biological Weapons Convention (BWC). According to Russian colleagues, more than 10,000 scientists are still associated with institutions of the former Soviet BW complex, with an estimated 1,500 having the high-level skills necessary to carry out work on dangerous pathogens.[1] Thus, the program will involve a substantial proportion of the leading specialists of interest. If all U.S. efforts in this field are well coordinated, joint projects could engage most of the leading defense scientists.
- The committee believes that the pool of U.S. specialists is sufficiently large that appropriate collaborators will be available to participate in a program of this size. Each U.S. collaborator will receive an average of $165,000 for the three-year period. It is assumed that one-half of the U.S. collaborators will host research visits of 3 to 12 months by Russian colleagues and one-half will send postdoctoral

[1] Well-informed senior Russian specialists advised the committee that of the 9,000 scientists in the Biopreparat complex; about 1,000 could be considered highly skilled senior researchers with considerable experience related to dangerous pathogens. Other well-informed Russian scientists stated that between 150 and 200 scientists are currently working on biological defense issues at MOD facilities. Still others contended that there are several hundred senior researchers at the plague institutes and other civilian facilities who previously conducted work related to dangerous pathogens with financial support from MOD.

scientists or graduate students to Russia for 3 to 6 months by drawing on these funds. The principal investigator and collaborator will also make exchange visits, and the funds will cover these costs as well as provide some salary and overhead reimbursement. Some projects will involve long-term exchanges in both directions, some will call for one-way long-term exchanges, and others will include only short-term exchanges of one to several weeks. In any event, the desirability of long-term exchanges involving serious side-by-side research is clear. Some U.S. institutions, such as USAMRIID and CDC, can provide collaborators for a limited number of projects. Other U.S. organizations, particularly universities, will serve as hosts for most of the projects. In this regard, a special effort is needed to ensure that the U.S. research and development community is aware of the *Pathogens Initiative* and that interested scientists from many institutions have the opportunity to apply to participate in the programs developed.

In short, focused joint research activities of this magnitude will make a substantial contribution to public health and national security and will concentrate research on dangerous pathogens at carefully selected facilities in each country.

Framework for the Effort

The committee recommends clustering collaborative research projects in the following seven program areas:

1. anthrax,
2. melioidosis and glanders,
3. plague,
4. orthopox viruses,
5. viral hemorrhagic fevers,
6. other dangerous pathogens and diseases of public health concern, and
7. cross-cutting basic research related to dangerous pathogens.

The first five areas are directed to important agents and diseases historically linked with BW activities. In each of these areas, Russian institutions are believed to have invested significant resources in research that has been largely unknown outside Russia.

The sixth program area will provide opportunities to address other pathogens and diseases of public health concern. Some pathogens of broad public health interest, such as *Francisella tularensis*, may be of BW concern, whereas others, such as those that cause tuberculosis and influenza, may not be historically associated with BW. This program area is particularly important in permitting key defense scientists who are interested in addressing problems unrelated to BW to participate. It will also expand the pool of potential U.S. collaborators beyond the limited number of scientists engaged in research on agents of BW concern. In addition, this area may increase the possibilities for commercially viable activities.

Similarly, the seventh program area provides additional opportunities for cooperation in fundamental research related to a variety of dangerous pathogens or diseases, with immunology being an example of an area of interest.

The committee's selection of these program areas followed consultations with Russian colleagues who provided assurances that these areas are of interest to Russia. They anticipate that if an expanded cooperative program is undertaken the concurrence of the Russian government about these specific areas will be forthcoming.

Russian colleagues have proposed that joint Russian-U.S. teams meet to develop comprehensive approaches for addressing pathogen-specific program areas. Their concept, set forth by representatives of Biopreparat during the June meeting in Moscow, is that each program area should include projects at several institutes concerned with epidemiology, studies of strain variations, identification and diagnostic techniques, prophylaxis and treatment techniques, and application of research findings. They have

suggested including within each program area a jointly agreed-upon list of candidate projects costing up to $5 million for the participating Russian institutions over a period of five years. They recognize that funds probably will not be available to support all proposed activities within the $5 million ceiling.

The committee considers the Russian proposal a good point of departure for further discussion of the scope and priorities of the pathogen-specific program areas. In addition to clarifying scope and priorities, joint teams should play a useful role in encouraging the development of specific proposals by institutions in both Russia and the United States that fit within the agreed-upon program frameworks.

Also, the joint teams should ensure that the Russian institutions being considered for participation in the program have the capability to provide and maintain laboratories at an adequate level. Many laboratories are currently in a state of disrepair and are frequently deprived of necessary power, water, and supporting services; substantial Russian investments are necessary if such laboratories are to be involved in the program. As previously noted, projects should be located only at facilities capable of carrying out the proposed activities; any rehabilitation of facilities is the financial responsibility of the institution proposing the project.

In any event, individual project proposals should be considered through appropriate review mechanisms in both countries on a project-by-project basis. Those that are most important, in accordance with the criteria set forth in Chapter 2, should receive funding first. There is no reason to divide available funds equally among the seven areas. Indeed, division of funds should depend largely on the quality of the project proposals in competition with each other across program areas.

Finally, the existing pilot projects should be incorporated into the program within the context of the program areas described. These projects were intended to provide early results on a limited scale and represent truncated versions of longer-term projects initially proposed by the Russian institutes. All received favorable evaluations, and some have good potential for long-term sustainability. Some or all of the projects may produce results that justify continuation beyond their scheduled termination dates in 1998.

Involving Additional Russian Institutions

If MOD indicates interest in participating in the program, the exploration of possible collaborative projects involving its institutes should receive high priority. The program also should be prepared to support MOD specialists working at Biopreparat institutes or as subcontractors to Biopreparat institutes if appropriate projects are proposed.

Several Biopreparat research institutes, in addition to the two that are carrying out pilot projects, have significant capabilities and should become involved in the program. For example, the Institute of Immunology in Lyubuchany, the Institute for Highly Pure Biopreparations in St. Petersburg, and the Institute for Scientific Biological Instrumentation in Moscow are believed to have strong capabilities and have expressed interest in collaborative projects; they may be considered early candidates for projects. Other institutes are identified in Boxes 1-2, 1-3, and 1-4.

The possibility of including Russian engineers and technical personnel who played key roles in designing the processes and equipment used in the former Soviet BW program should be explored. Their involvement in collaborative activities could help open opportunities for joint efforts to reconfigure former BW facilities under the Cooperative Threat Reduction (CTR) program. Alternatively, such technical personnel may be more appropriate participants for other U.S.-sponsored programs, such as the IPP. The *Pathogens Initiative* could provide brokering services for U.S. programs that do not have comparable contacts within the Biopreparat establishment. In this regard, Biopreparat facilities at Omutninsk, Pokrov, and Berdsk and engineering research institutes in Moscow and Kirov have indicated interest in collaborative activities; their scientific and engineering potential deserves careful attention.

A special opportunity to engage previously isolated specialists from Biopreparat and MOD facilities may exist in Kirov. The recently established Volgo-Vyatka Applied Biotechnology Center, which served as host for the international symposium in the Kirov region in June 1997, is well positioned to provide introductions to several important MOD and Biopreparat institutions in the region. Also, Biotin, a major Biopreparat biochemical production enterprise with extensive contacts in the region, has indicated an interest in joint projects. A follow-up visit to Kirov in the near future may be a useful step toward broadening Russian participation in the *Pathogens Initiative* and related engineering efforts.

The Plague Research Institutes in Saratov and Stavropol have indicated interest in participating in cooperative activities, and on-site visits by U.S. experts are needed to carefully assess their capabilities. At a later date, assessments of the capabilities of the three other plague research institutes in Russia also should be considered.

Finally, as suggested in previous chapters, efforts should be considered to link former Soviet BW facilities and civilian institutes in common projects. There are a number of well-known civilian institutes with relevant research interests in the Ministry of Health, the Russian Academy of Medical Sciences, the Russian Academy of Sciences, and the Russian Academy of Agricultural Sciences; they should be encouraged to cooperate with former Soviet BW facilities as appropriate. Although the past capabilities of most of the civilian institutes are well known in the West, visits to these institutes are needed to better appreciate their current capabilities after extensive losses of personnel and aging of equipment.

Supporting Activities

Improvement of the electronic communications capabilities of Russian institutions participating in joint projects is important for meaningful international collaboration. Communications upgrades for Russian participants can be built into large projects or clusters of small projects at the same location. Installation costs of such upgrades depend on the specific institution and could range from thousands of dollars for computers, modems, and links to local telephone circuits to hundreds of thousands of dollars for satellite facilities at remote locations such as Koltsovo. Operating expenses also must be considered because e-mail and Internet services can be costly for impoverished institutions. Given the importance of this topic and the specialized nature of an authoritative assessment of needs, early joint assessment of electronic communications capabilities within the Biopreparat complex by well-qualified experts is important. The primary focus should be on institutes with strong potential for participating in sustained collaborative efforts.

In yet another area, both the Saratov Plague Institute and the Ivanovsky Institute for Virology have proposed projects for upgrading the safekeeping and utility of their strain collections, which serve as standards for the country. The Gamaleya Institute of Epidemiology and Microbiology also has national reference collections of strains, and the Chumakov Institute for Poliomyelitis and Viral Encephalitides holds a reference collection in its field. A number of other institutes have specialized collections. Russian institutes with standard reference collections or other significant collections should be encouraged to prepare project proposals for more effective utilization and maintenance of the strains; those that receive high evaluations should be considered for support. An important aspect of collaborative projects concerning pathogenic strains should be the procedures that are in place or that will be adopted to ensure transparency about how these strains are to be used. Such transparency should help ensure that the projects undertaken not contribute to activities that violate international obligations pursuant to the BWC. Although Russia has many regulations governing the handling and use of strains, the details of such regulations are not widely known outside the country. A comparison of recently promulgated U.S. and Russian regulations should be considered as a topic for a workshop or a joint project.

Finally, exchanges of information about the biosafety regulatory frameworks for handling dangerous pathogens in the two countries began during initial consultations with Russian colleagues. Box

3-1 lists some of the relevant Russian laws and regulations. Because such regulations are still evolving in both countries, periodic reviews should be held of requirements that could impinge on cooperative programs. Of particular interest would be early workshops to consider the following issues: registration of high-hazard laboratories, control over collections of strains of dangerous pathogens, setting and monitoring standards biosafety, and procedures for controlling the movement of dangerous pathogens within a country and between countries.

Box 3-1 Selected Russian Laws, Decrees, and Regulations on the Control of Dangerous Pathogens

- Decree of the Russian President on ensuring the fulfillment of international obligations in the area of biological weapons, April 11, 1992 (Decree 390)
- Procedures for controlling export from the Russian Federation of disease agents, their genetically altered forms, and fragments of genetic material that can be used for developing bacteriological (biological) and toxin weapons, November 20, 1992 (Decision of the Russian Government, No. 892)
- Licensing and establishing quotas for exports and imports of biological goods and services, included in instructions of the State Customs Committee, No. 610 of December 12, 1992
- Federal law on state regulation in the area of genetic engineering, June 5, 1996 (adopted by the state Duma)
- Safety of microorganisms of Group I-II pathogenicity, sanitary regulations of 1994, Sanitary Epidemiology Service of Russia
- Interim regulations concerning dangerous work with recombinant DNA, Scientific Center for Biological Research of the Soviet Academy of Sciences, Pushchino, 1978 (prepared by an interagency council)
- Penalties for crimes against the peace and security of mankind: Production or proliferation of weapons of mass destruction, Sections 355 and 356 of the Russian Criminal Code of 1996.

NOTE: These laws, decrees, and regulations have been identified by Russian specialists as being of particular relevance to bilateral cooperation directed to research on dangerous pathogens.

Project Development Activities

During the early years, a variety of activities will be particularly important in developing proposals for joint research and in matching appropriate collaborators. Annual reviews of ongoing projects can help guide selection of future high-priority research themes. Also, the overall approach should be reviewed in depth at the end of the second year and adjusted as necessary.

In addition, the following types of project development activities should be carried out:

- Brief exchange visits to enable researchers from the two countries to develop proposals for submission to funding competitions;
- Travel grants for Russian scientists to participate in scientific conferences in the United States, where they can make contacts and become aware of the state of international science in their fields; and
- Joint scientific workshops to explore new areas for possible projects, including workshops that build on the results of completed projects.

Estimated Cost

The estimated annual cost to the United States of a *Pathogens Initiative* is $6.0 million in the first year (FY 1998), $7.0 million in the second year, and $8.5 million per year in the third, fourth, and fifth years. The steady-state annual costs for the final three years will be as follows:

- Four and a half million dollars (53 percent) to support 15 new projects each year at Russian research institutions throughout the three-year project lifetime. The total funding of $4.5 million will be committed at the beginning but disbursed over the course of the projects. Disbursement, of course, will depend on performance in accordance with agreed-upon work plans.

- Two and a half million dollars (29 percent) to support U.S. collaborators and exchange visits associated with the 15 projects for three years, with the entire amount of funds again committed but not disbursed at the beginning.
- One-half million dollars (6 percent) to support (1) panels of U.S. experts to review project proposals, (2) joint U.S.-Russian workshops to identify priority areas for collaboration, and (3) exploratory visits by U.S. specialists to Russian institutions with largely unknown capabilities, including, if possible, MOD institutes.
- One million dollars (12 percent) for program evaluation, financial management, and related support activities for the *Pathogens Initiative*, involving three full-time staff members.

During the first two years of the *Pathogens Initiative*, project costs will be lower and project development costs will be higher. Thus, the recommended funding level of $6 million for FY 1998 assumes that only 10 projects are initiated; the level of $7 million for FY 1999 assumes 12 projects, leading to 15 new projects in each of the final three years at an annual cost of $8.5 million. (Table E-3 lists the allocation of funds per fiscal year.) The Russian financial contributions will cover primarily (1) the pension, health, and related benefits packages for Russian participants and (2) indirect project costs incurred at Russian facilities because the U.S. overhead contribution will be only about 7 percent of the total project costs. In addition, Russian waivers of value-added taxes and personal income taxes, in a sense, place a financial burden on the Russian government.

Anticipated Results

The foregoing approach will represent a significant commitment by both the United States and Russia to expand research activities and exchange information on biosafety controls over dangerous pathogens. As such, it would advance both the national security and the public health agendas of the two countries. Also, invited efforts would be significant in setting the stage for sustained long-term efforts after the five-year initiative.

The *Pathogens Initiative* is designed to help reduce the likelihood of proliferation of dangerous technologies that are extremely difficult to control, to encourage a concentration of Russian activities at carefully selected facilities with high scientific potential, and to encourage reconfiguration of former Soviet BW facilities to address new public health challenges. It also should contribute to building confidence at the government and laboratory levels about the legitimacy of activities that are under way.

4

◆ ◆ ◆ ◆ ◆

Phase 2: An Era of Sustained Cooperation

THE UNCERTAIN FUTURE OF RUSSIA

Predicting conditions in Russia 5 to 10 years into the future is uncertain. Russia's national security apparatus, its economic reform agenda, and even its system of political governance are under considerable stress; changes in all of these areas are likely. Depending on the character of such changes, the consequences for defense scientists and public health activities in that country could be substantial. Program recommendations for the distant future concerning national security and public health issues thus should be flexible.

At the same time, U.S.-Russian relations are continually evolving, with bilateral cooperation in areas of national security being particularly sensitive to the state of political relations. In addition, bilateral cooperation directed toward dangerous pathogens cannot be isolated from diplomatic progress in resolving disagreements about compliance with the Biological Weapons Convention (BWC). The committee believes that an ideal outcome involving the BWC and expanded bilateral cooperation would be a synergistic effect, with high-payoff scientific cooperation improving the climate for diplomatic progress and improved political understanding paving the way for broader scientific interaction. The bilateral cooperation envisaged would be a tangible manifestation of U.S. and Russian commitments to Article X of the BWC, which calls for cooperation in the prevention of diseases.

Another area of uncertainty is the future interest of countries in addition to the United States and Russia in a global approach for expanding activities directed toward dangerous pathogens. Whatever the level of interest, however, there is no substitute for U.S. leadership in encouraging Russia to adopt transparency measures, such as those described below, for a broad range of facilities and activities. Thus, efforts to globalize activities should be welcomed, but they are not a substitute for strengthening U.S.-Russian cooperation.

A MODEL FOR SUSTAINED COOPERATION

Despite the foregoing uncertainties, the committee decided to offer a model of a desirable and realistic program of sustained bilateral cooperation. Such a model, referred to here as Phase 2, could provide a goal toward which U.S. and Russian officials and specialists can direct their energies. Ideally, as the *Pathogens Initiative* carried out during Phase 1 approaches its end in fiscal year (FY) 2002, the enthusiasm in both countries for bilateral cooperation should have reached such a high level that Phase 2 activities can build on past successes without interruption.

Development of this model does not mean that the *Pathogens Initiative* would be useful only if a Phase 2 program develops beginning in 2003. Indeed, the benefits of the *Pathogens Initiative* identified in previous chapters should be realized in both Phase 1 and Phase 2. At the same time, a Phase 2 program could enable the two countries, as well as others, to utilize these benefits more fully and make additional contributions to international security, economic development, public health, and international science.

ORGANIZATIONAL ARRANGEMENTS FOR A PHASE 2 PROGRAM

If bilateral cooperation develops rapidly as a result of the *Pathogens Initiative*, the intergovernmental coordinating mechanism suggested in Chapter 3 becomes increasingly important. During Phase 2, a formal structure for intergovernmental coordination would be essential.

One approach for Phase 2 would be to establish an intergovernmental commission, supported by national coordinating bodies, to guide and coordinate cooperative efforts related to dangerous pathogens. The national security and public health aspects of a significantly expanded program of cooperation appear sufficiently important to warrant consideration of a commission dedicated exclusively to this topic. Although the two governments might decide to use another approach, for the purposes of this discussion it is assumed that a commission would be the coordination mechanism of choice.

From the beginning, the commission would be aware of all joint programs involving dangerous pathogens, but it would be committed to facilitating, not complicating, implementation of previously existing bilateral programs. The commission would be responsible for a variety of activities such as the following.

- Establishing priorities and providing overall guidance for all aspects of cooperation—both new and existing activities—and, on a selective basis, reviewing and evaluating progress in implementing activities of special interest
- Approving new cooperative activities
- Making financial commitments for cooperative activities
- Ensuring coordination between new projects and related existing projects and assisting the arrangement of logistics support
- Disseminating both scientific reports and public information about activities of broad interest
- Developing bilateral arrangements that address issues such as intellectual property rights, mechanisms for the rapid importation of essential equipment and supplies, and living accommodations for visiting scientists and their families.

Much of the technical work of the commission would be carried out by bilateral expert groups in areas such as research cooperation, joint efforts in epidemiology, and common requirements for biosafety. Some topics of likely interest to such groups are addressed later in the discussion of technical aspects of the program.

The national coordinating body in the United States should build on experience during the *Pathogens Initiative,* which calls for collaborative efforts of the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), Centers for Disease Control and Prevention (CDC), National Institutes of Health (NIH), Food and Drug Administration (FDA), U.S. Department of Agriculture (USDA), and nongovernment sector. Coordination of bilateral and multilateral activities would probably require greater attention during Phase 2. Also, linkages with joint efforts on other public health concerns should be strong.

GENERAL CHARACTERISTICS OF PHASE 2

Given the legacy of mutual mistrust in this field, an era of sustained cooperation should emphasize transparency at several levels. Building on the initial experience in implementing transparency arrangements associated with specific joint projects, Phase 2 would call for broader transparency arrangements for handling dangerous pathogens at the institutional and national levels, as well as at the project level.

A number of components of the Phase 2 program would build on early experience gained within the framework of the *Pathogens Initiative*. Therefore, details of these activities should be modified as

such experience accumulates. Some of the suggested components of Phase 2 may be incorporated at an earlier date into the *Pathogens Initiative* if cooperation develops more rapidly than anticipated.

When fully developed—perhaps in 7 to 10 years—the Phase 2 program would provide a framework for cooperative activities in many aspects of the handling and use of dangerous pathogens in both countries. It would be sufficiently broad in scope that any research, development, or production group with interests in dangerous pathogens in either country would be eligible to participate in cooperative projects. The scientific activities of research teams in both countries would be reported regularly, and the teams would welcome visits to their facilities and detailed discussions of their activities whenever possible. Cooperation would include joint projects at high-hazard facilities and visits by foreign specialists to familiarize themselves with such facilities. It also would include joint efforts to protect and account for any strains of infectious agents that are of mutual interest. Finally, cooperation in biosafety could help ensure that activities involving dangerous pathogens are being handled responsibly in both countries.

The need to protect intellectual property rights and control the dissemination of information that is sensitive because of potential application to biological weapons (BW) is clear. Such requirements, however, should not unnecessarily exclude activities from consideration when cooperative programs are being developed.

By the time Phase 2 is being implemented, the parties to the BWC may have adopted a verification protocol; in this case, procedures concerning access to facilities and information of all types might already have been specified. Such procedures could serve as guidance for implementation of the broadly based program envisaged during Phase 2. If such a protocol is not in place, the commission suggested earlier would be even more important and would have to develop procedures on its own to expand the scope of transparency developed during the *Pathogens Initiative*.

Joint research projects would continue to be the core of activities under the purview of the commission. However, another key aspect in addressing both political and scientific concerns would be steps in both countries to promote effective national regulations for controlling dangerous pathogens. Effective enforcement procedures and sharing of experiences would be particularly important in confidence building.

Over time, the commission would seek to establish additional confidence-building measures. In particular, its goal would be the development of rules to govern a comprehensive exchange of information between the two countries on the handling and use of dangerous pathogens. Ideally, the general characteristics of all significant research and related facilities involved with dangerous pathogens in both countries would be known to each government. The activities of research teams would be regularly reported, as would the strains of infectious agents held for research and related purposes. As with the cooperative activities proposed, measures to ensure adequate protection of intellectual property and other sensitive information in a manner that does not undercut the broader transparency objectives should be developed.[1] Currently, such comprehensive exchange of information is difficult if not impossible to achieve, but as trust between the two countries grows, greater openness should become possible. Moreover, because of concerns about biosafety and terrorism, there is increasing government interest, at least in the United States, in developing such requirements for reporting to national authorities. Thus, there may be both an international and a national basis for bilateral confidence building through expanded exchanges of information.

[1] For example, in the United States a mechanism for protecting proprietary chemicals and providing adequate information for regulatory purposes is well developed and may serve as a precedent for application in the field of biology.

TECHNICAL ASPECTS OF THE PROGRAM

The following sections describe specific approaches in several areas, together with an estimate of their implementation costs to the U.S. government beyond current investments. Adjustment of some of these suggestions and of the cost estimate will inevitably emerge during more detailed program discussions within the U.S. government and with Russian officials.

Research Collaboration

Specialists representing the scientific interests of both countries would meet at least annually to develop agendas for joint research projects for subsequent approval by the two governments. When Phase 2 reaches maturity, the research program would probably be somewhat larger than that of the *Pathogens Initiative*, perhaps 30 percent. Growth to this level is based on several considerations. First, some Russian specialists likely will continue to play key roles in legitimate military research activities during the *Pathogens Initiative* because they are reluctant to abandon their assured sources of income for participation in an international program that may be only temporary. However, after five years of continuous collaboration, these specialists should recognize the importance and sustainability of the program, and some could be expected to become applicants for participation in an expanded program. Second, interest in the United States should grow, particularly if the *Pathogens Initiative* is successful in attracting young U.S. specialists who experience firsthand the benefits of international scientific cooperation. Although the committee supports modest growth, it believes that the program should be capped to ensure the high quality of the projects supported. As noted in Chapter 3, this maximum level of activity is driven by both the importance of limiting the number of facilities involved in work on dangerous pathogens and the manpower pools of specialists available in the two countries to address important public health issues in a highly specialized field.

The following approach, which could be formally established by the commission, appears appropriate for the expanded program during Phase 2:

- Annual or semiannual competitions should be held among Russian institutions and investigators for financial support for projects, including review of applications for support of research on selected pathogens as in the *Pathogens Initiative.* Other dangerous pathogens and cross-cutting research projects that individual investigators propose for support would probably receive much greater emphasis.
- Joint U.S.-Russian peer review panels should be established to select projects for support.
- Final government approvals should be obtained and arrangements made for financial support, including limited U.S. support for Russian activities through the International Science and Technology Center (ISTC) as discussed below or through an equally effective mechanism if the character of the ISTC were to change in the years ahead.

Epidemiology

During Phase 2, special attention would be given to research related to the epidemiology of diseases associated with dangerous pathogens, although some activities might be initiated on a limited scale during Phase 1. Combined capabilities in this field should have major public health benefits in combating the spread of diseases both nationally and worldwide through the following mechanisms.

- Rapid exchanges of significant information on trends and unusual occurrences of diseases associated with dangerous pathogens in the United States and Russia are very important. Some Russian institutions require additional electronic equipment for such communication, and this need should be considered within the context of specific joint projects, as discussed in Chapter 3. Also, joint workshops

would be useful in developing a general consensus on the frequency of and mechanisms for data exchanges and the variety and format of data to be exchanged. This effort should be consistent with the interests of the World Health Organization (WHO), and should support its *Weekly Epidemiology Reports*.

- Related to the international exchange of data is the need to strengthen the internal capabilities of Russia to rapidly assess and process information about disease trends and outbreaks. Projects that enable selected institutes, particularly key members of Biopreparat, to contribute to the national effort of the Ministry of Health should be considered.
- Bilateral workshops and joint research projects should be directed to identifying and developing improved technologies for the diagnosis of agents and diseases of concern.
- During outbreaks in one country of certain diseases linked with dangerous pathogens, specialists in the other country should be encouraged to forward relevant information and identify ways in which they could be most helpful in assessing and responding to such outbreaks. When appropriate, specialists from the other country would be invited to review information and assist in assessments if they have special expertise that could be helpful.
- Russian specialists who are involved in field investigations should be encouraged to apply for participation in CDC training programs.

Research projects related to epidemiology that involve both former Soviet BW institutes and civilian institutions, (for example, institutes of the Biopreparat complex teamed with those of the Ministry of Health or Academy of Medical Sciences) are of special interest. Indeed, strengthening internal organizational linkages within Russia is essential if its defense scientists are to play a significant role in the national public health effort.

Biosafety

The objective of efforts in both countries in the area of biosafety would be to promote consistency in biosafety criteria and practices research laboratories or other facilities that handle dangerous pathogens. Such efforts would help provide assurance (1) that infectious agents are handled in conformance with the WHO *Laboratory Biosafety Manual*[2] and (2) that infectious agents are not transferred to parties who are not authorized to handle them. Also, ensuring that regulations for vaccinations and biosafety procedures are consistent will facilitate reciprocal visits to high-hazard laboratories.

The commission should concentrate on reviewing the development, implementation, and enforcement of national systems in the United States and Russia for controlling the handling and use of dangerous pathogens. It should encourage each government to develop and use approaches that are both effective and transparent, thereby contributing to mutual confidence about compliance with international obligations.

In considering the regulatory framework, the commission might examine, for example, the working lists of infectious agents already set forth in regulations and guidance documents, procedures for registering facilities with national authorities, national requirements for transferring agents nationally and internationally, biosafety criteria for facilities, requirements for disposal of agents, and training of scientists and support personnel.

Among the mechanisms for cooperation related to biosafety are the following approaches:

- Regular exchanges of information on the state of development of national regulatory systems;
- Special exchanges of data on specific activities of particular interest to each country, such as research being carried out at biocontainment or other specialized facilities; and

[2] World Health Organization. 1993. *Laboratory Biosafety Manual,* 2nd Ed. Geneva: WHO.

- Reciprocal visits to selected facilities by biosafety experts on the basis of invitation.

ESTIMATED COSTS

It is expected that as Phase 2 is developed, the Russian participating institutions will be in a position to pay increasingly more of their costs of these cooperative activities. Also, an orderly transition between funding of the *Pathogens Initiative* and financial support for projects in Phase 2 is recommended. In particular, as indicated in Table E-2, the funding of three-year projects during the last two years of the *Pathogens Initiative* should provide an important base of activities for the first two years of Phase 2. The time needed for full development of Phase 2 depends in large measure on the Russian economy and the priority given to efforts directed toward dangerous pathogens.

Because the Russian economy will probably remain weak for a decade or more, U.S. support will be necessary for some Russian activities. In particular, U.S. contributions to Russian expenses might concentrate on (1) purchases of specialized equipment and supplies for experiments in Russia that are directly linked to experiments in the United States and (2) international travel of selected Russian participants who otherwise might not be able to travel to the United States. However, U.S. funds should be used primarily to cover the costs of U.S. participants.

Without considering inflation, the cost to the United States of carrying out activities during Phase 2 is estimated at approximately $10 million per year. About $5 million (50 percent) would support the expenses of U.S. collaborators, with each of an estimated 60 collaborators (20 new collaborators undertaking three-year projects each year) receiving an average of $80,000 per year for their activities. An additional $2 million (20 percent) would be for administrative expenses related to U.S. participation in the commission and its expert groups, which would have five full-time staff members. About $1 million (10 percent) would be used for workshops, project development activities, and planning and evaluation meetings between Russian and U.S. specialists. The remaining $2 million (20 percent) would support the requirements of Russian specialists that are beyond their own means: small pieces of equipment for experiments of special interest to the United States and associated project related international travel for some participants (at an estimated cost of $35,000 per year per project).

Sustained U.S. funding for Phase 2 would undoubtedly require agreement between the executive branch and Congress on a line item in the budget of a selected agency. It is premature to speculate which agency should have financial responsibility.

ANTICIPATED BENEFITS

The Phase 2 program would provide financial, scientific, and information-sharing incentives for the two countries to broaden and sustain linkages between their specialists. The impact of specific joint efforts on public health and other problems is difficult to predict, but Russian and U.S. specialists are in a strong position to contribute substantially in this area of increasing worldwide concern.

A likely effect of a sustained program would be adjustment of the structure of the Russian research enterprise dealing with dangerous pathogens. Research projects would be increasingly concentrated at a handful of the best institutions in the country that emerge as centers of excellence. Some weaker institutions would slowly lose their ability to conduct research on dangerous pathogens and would have even greater difficulty commanding financial support for such work than during the current crisis period.

Special efforts would be necessary to ensure that the stronger institutions are prepared to absorb some scientists from the weaker institutes lest they be tempted to transfer their know-how to states of

proliferation concern. Although consolidation in the Russian research complex would appear to be inevitable, such consolidation should be carefully managed.

If the United States and Russia are able to work together constructively over the long term, the tone of international diplomacy in this field could be significantly improved, resulting in new and important mitigation of the threat of proliferation and terrorism and improved U.S.-Russian relations in an area that too frequently has been punctuated with acrimony. In addition, long-term joint efforts would make major contributions to reducing global risks from emerging and reemerging infectious diseases.

A
Committee and Staff Biographies

COMMITTEE MEMBERS

Joshua Lederberg (NAS, IOM), *chair*, is Professor Emeritus and Raymond and Beverly Sackler Foundation Scholar at the Rockefeller University. In 1958 he received the Nobel Prize in Physiology or Medicine for his work in bacterial genetics. He has been active in many national and international science policy deliberations, especially at the National Institutes of Health (NIH) and World Health Organization (WHO). He served as a consultant to the Arms Control and Disarmament Agency during negotiation of the 1972 Biological and Toxin Weapons Convention (BWC), and he currently serves on the Defense Science Board.

John D. Steinbruner, *vice-chair*, is a Senior Fellow and former Director of the Foreign Policy Studies Program at the Brookings Institution. He has held faculty positions at Yale University, Harvard University, and Massachusetts Institute of Technology. A political scientist, he has written extensively on arms control and security issues, including problems of command and control and crisis decision making. He is a member of the Defense Policy Board.

Barry Bloom (NAS, IOM) is Investigator at the Howard Hughes Medical Institute of the Albert Einstein College of Medicine. He has received numerous awards for his work in immunology and infectious diseases, including the Bristol-Myers Squibb Award. He has been active in the programs of WHO.

Gail Cassell (IOM) is Chair of the Department of Microbiology and Charles H. McCauley Professor of Microbiology at the University of Alabama-Birmingham. She has received a number of awards for her research in infectious diseases and is a recent past President of the American Society for Microbiology. She has been active in national and international policy deliberations, including those of NIH and the U.S.-Japan Cooperative Medical Science Program. She is also a member of the International Science and Technology Center Science Advisory Committee and a member of the steering committee for the U.S.-Japan Cooperative Medical Science Program. She is a recent chair of the Board of Scientific Counselors of the National Center for Infectious Diseases of the Centers for Disease Control and Prevention (CDC).

Robert Chanock (NAS) is Chief of the Laboratory of Infectious Diseases of the National Institute of Allergy and Infectious Diseases of NIH. He has received numerous awards for his work in virology and infectious disease research, including the Bristol-Myers Squibb Award for Distinguished Achievement in Infectious Disease Research, the Robert Koch Medal of the Robert Koch Foundation, the ICN International Prize in Virology, and the Albert Sabin Gold Medal of the Albert Sabin Vaccine Foundation. He has been active in WHO and in national policy discussions.

R. John Collier (NAS) is Professor of Microbiology and Molecular Genetics at Harvard Medical School. His career has been largely devoted to research on the structures and actions of bacterial toxins. He has received a number of awards during his career including the Eli Lilly Award in Microbiology and Immunology and the Paul Ehrlich Prize.